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EXAMINER	
PAGONAKIS, ANNA	
ART UNIT	**PAPER NUMBER**
1614	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/586,841	DAYAN, DAN	
	Examiner	Art Unit	
	ANNA PAGONAKIS	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 August 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28-52* is/are pending in the application.

4a) Of the above claim(s) *28-46* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *47-52* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4 sheets, 10/2/2006; 3 sheets, 7/20/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's election with traverse of hydroxychloroquine and chlorhexidine in the reply filed on 8/4/2008 is acknowledged. The traversal is on the ground(s) that the cited reference contains different compounds and different disorders. This is not found persuasive because the instantly claimed compounds are in fact quinoline derivatives (see instant claim 1) which are used to treat different disorders than the instantly claimed ones, thereby providing the technical feature.

The requirement is still deemed proper and is therefore made FINAL.

Claims 28-52 are pending in the application. Claims 28-46 withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected subject matter, there being no allowable generic or linking claim. Accordingly, claims 1-27, 53 have been cancelled, claims 28-46 have been withdrawn, claims 47 has been amended.

This application is the national stage entry of PCT/IL05/00078 filed 1/21/2005; and claims benefit of foreign priority document ISRAEL 160022 filed 1/22/2004; ISRAEL 161012 filed 3/22/2004; ISRAEL 162591 filed 6/17/2004; currently English translation of these foreign priority documents have been filed.

Claims 47-52 are currently under examination and the subject of this Office Action.

Information Disclosure Statement

The information disclosure statement filed on 10/2/2006 and 7/20/2006 have been received. Documents with no publication date provided were not considered.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 47-52 are rejected under 35 U.S.C. 112, first paragraph, because while the specification is enabling for treating canker sores, apthae and erosions/ulcerations (see examples of pages 14-18 of instant specification), does not reasonably provide enablement for prevention of these conditions. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope of these claims.

Attention is directed to In Re Wands, 8 USQP2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing Ex parte Forman, 230 USPQ 546 (BdAppls 1986) at 547 the court recited eight factors: (1) the nature of the invention, (2) the breadth of the claims, (3) the relative skill of those in the art, (4) the state of the prior art, (5) the predictability of the art, (6) the amount of direction or guidance provided, (7) the presence or absence of working examples, and (8) the quantity of experimentation necessary.

The instant specification fails to provide guidance that would allow the skilled artisan to practice the instant invention without resorting to undue experimentation, as discussed in the subsections set forth infra.

1) the nature of the invention. The invention discloses a derivative for the treatment and prevention of oral mucosal disorders.

2) the breadth of the claims. The claims are broad because they read on "prevention."

3) the relative skill of those in the art. The relative skill of those in the art are PhD, MD and MS.

4) the predictability or lack thereof in the art. Prevention is not practical with oral diseases due to the unpredictability of the condition. Periodontal disease begins with plaque that is not removed during daily cleaning. When plaque is not removed it turns into calculus. It is impossible to remove all calculus with daily brushing (www.perio.org/consumer/farq_general.htm, page 1-4). The calculus, if untreated,

causes gingivitis, the first stage of periodontal disease. Therefore, it is likely a small amount of gingivitis is present in between dental visits.

5) the amount of direction or guidance present. The disclosure teaches treatment of oral mucosal diseases such as canker sores, apthae and erosions/ulcerations but lacks any type of guidance that would lead one to believe that prevention of the oral diseases from forming again or occurring all together is possible. This guidance or lack thereof is not commensurate with the full scope of the claims.

6) the presence or absence of working examples. The examples in the specifications are examples where a patient is treated for canker sores, apthae and erosions/ulcerations using chlorhexidine and hydroxychlorquine. There is a lack of working examples showing the prevention of canker sores, apthae and erosions/ulcerations comprising chlorhexidine and hydroxychloroquine.

7) the quantity of experimentation needed. The applicant needs to provide examples using chlorhexidine and hydroxychloroquine that are likely to develop oral mucosal disorders. Other experiment include patients who have had oral mucosal disorder and no longer have it, and show that they do not develop the disease or condition related to the disease again.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 47-52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Burgess et al (Drugs, 39(1), 1990) and Worle et al (British Journal of Dermatology, 137, 262-265, 1997).

Burgess et al. teach chlorhexidine has been found to reduce ulcer pain and duration and may reduce secondary infection in some individuals with minor aphthous (page 56, second column).

Worle et al. teach that chronic ulcerative stomatitis has recently been described as a new disease entity characterized by chronic ulceration of oral mucosa which responds to treatment with hydroxychloroquine.

One of ordinary skill in the art would have found in prima facie obvious to combine the chlorhexidine taught by Burgess et al. and the hydroxychloroquine of Worle et al. because both agents are known to have efficacy in oral ulcer mucosa disorders. Motivation to do so flows logically from the very fact that that each was known in the prior art to have the same therapeutic utility and, in turn, raises the reasonable expectation of success that the two therapies, when combined, would have, at minimum, additive, if not synergistic, oral ulcer mucosal disorder treating effects when combined.

With respect to claims 48-52, the mode of administration of a specific ingredient in a composition is clearly a result effective parameter that a person of ordinary skill in the art would routinely optimize. Optimization of parameters is a routine practice that would be obvious for a person of ordinary skill to determine the optimal mode of administration to achieve the desired results from the claimed parameters, the optimization of ingredient amounts would have been obvious at the time of Applicant's invention. Further, the addition or removal of pharmaceutically acceptable excipients, diluents and adjuvants that have the optimum therapeutic index is well within the level of one having ordinary skill in the art. Accordingly, the artisan would have been motivated to determine optimum pharmaceutically acceptable excipients and adjuvants in order to get the maximum effect of the active agent.

The determination of a dosage and modes and methods of administration having the optimum therapeutic index while minimizing adverse and/or unwanted side effects is well within the level of the skilled artisan. Formulation of pharmaceutical compositions into different administrable preparations using a variety of carriers, excipients, diluents, solvents, binders or excipients was also a matter well

within the purview of the skilled artisan. The skilled artisan would have determined the optimum pharmaceutical formulation according to the pharmacologic effect desired. Particular pharmaceutical formulations known in the art at the time of the invention include hard or soft capsules, tablets, powders, granules, suspensions, syrups, emulsions or sprays (see Newmark et al. in U.S. Patent No. 6,242,012 at col.6, line 49-col.7, line 62), which could be prepared using any one or more of a variety of pharmaceutical additives, such as excipients, diluents, binders, lubricants or preservatives (see Newmarket al. at col.7, lines 8-19). The preparation of the active agent taught into any one or more of these known formulations and further comprising any one or more of the known pharmaceutical additives would have been obvious to the skilled artisan. Such a person would have been motivated to do so in order to optimize the efficacy of the pharmaceutical formulation.

Conclusion

No claim is found to be allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANNA PAGONAKIS whose telephone number is (571)270-3505. The examiner can normally be reached on Monday thru Thursday, 9am to 5pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

AP

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614